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10/031,036	01/15/2002	Wayne A. Bryden	1585-0002	4463

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Francis A Cooch  
The Johns Hopkins University  
Applied Physic Laboratory  
11100 Johns Hopkins Road  
Laurel, MD 20723-6099

EXAMINER

WEBER, JON P

ART UNIT PAPER NUMBER

1651

DATE MAILED: 01/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/031,036

Applicant(s)

BRYDEN ET AL.

Examiner

Jon P Weber, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 10 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) 15-25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-14 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. §§ 119 and 120

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☒ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

***Election/Restrictions***

Applicant's election without traverse of Group I, claims 1-14 in the Paper filed 10 November 2003 is acknowledged. Claims 15-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group, there being no allowable generic or linking claim. Election was made **without** traverse. It is suggested that the nonelected claims be canceled in response to this Office action.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "toxins of fungi" which lacks antecedent basis because it does not conform to a known genus, species or strain.

Claims 8 and 10 have an unknown symbol in front of "cyano" at line 2, which renders the compound asserted unknown. It is thought that "α" is the intended symbol.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-5 are rejected under 35 U.S.C. 102(e) as being anticipated by Eriksson et al.

(US 6,446,010).

Eriksson et al. (US 6,446,010) disclose analyzing peptide fragments obtained from a tryptic digestion of an unknown yeast protein sample by MALDI-TOF to create a database of masses for the peptides that can be compared to a database of yeast peptide masses for known proteins for identification of the unknown protein. The databases of known samples for various yeast proteins are generated in any manner that yields sufficient accuracy mass data.

Claim 1 is rejected under 35 U.S.C. 102(e) as being anticipated by Schnürer et al. (Jul 1999).

Schnürer et al. (Jul 1999) disclose identifying various fungal specific marker volatiles obtained from food spoiled by various fungi by GC-MS. As can be seen from Table 1, different volatile patterns are characteristic of different fungi.

Claims 1-3 are rejected under 35 U.S.C. 102(a) as being anticipated by Schneiter et al. (Aug 1999).

Schneiter et al. (Aug 1999) disclose ESI-MS/MS analysis of lipid compositions of yeast subcellular membranes. This is to be done with various individual species so as to better

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understand their function. Eleven different yeast subcellular membranes with *S. cerevisiae* was performed as a model study. Typically 20-100 scans were performed per analysis.

Claims 1-14 are rejected under 35 U.S.C. 102(a) as being anticipated by Welham et al. (Mar 2000) and Wellham et al. (15 Mar 2000).

Welham et al. (Mar 2000) disclose MALDI-TOF analysis of fungal spores to obtain a fingerprint of the proteins, glycoproteins, oligosaccharides and oligonucleotides of the intact cells. Several fungi were studied: *Penicillium spp.*, *Scytalidium dimidiatum*, and *Trichiphyton rubrum*. The purpose was to identify fungi on the basis of their characteristic patterns. Figures 2-3 shows several organic acid that were used in the matrices. The matrix further comprises 0.1% TFA. Mass spectra were averaged over 50-100 laser shots from a 337 nm nitrogen laser.

Claims 1-3 are rejected under 35 U.S.C. 102(a) as being anticipated by Jaworwski et al. (Apr 2000).

Jaworwski et al. (Apr 2000) disclose HPLC-ESI-MS to analyze peptaibol antibiotics antiamebins profiles from several filamentous fungi. The patterns are specific for each of the fungi.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by McCorkindale et al. (1969).

McCorkindale et al. (1969) disclose determining the types of sterols produced by different fungi by GLC-MS (See Table 2).

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Wilkins et al. (1996).

Wilkins et al. (1996) disclose determining the profiles of volatile metabolites produced by seven different actinomycetes by GLC-MS (See Table 1).

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Smedsgaard et al. (1996).

Smedsgaard et al. (1996) disclose using ESI-MS for secondary metabolite profiling of crude extracts from fungi. Ten different species could be discriminated on the basis of their secondary metabolite profiles (See Table 2). Generating a searchable database is suggested at pages 14-15.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Larsson et al. (1997).

Larsson et al. (1997) disclose identifying yeast proteins using MALDI-MS that have been resolved on a 2D electrophoresis gel. *Saccharomyces cerevisiae* is exemplified. The proteins for a specific yeast are thereby profiled. This can be done with other yeasts and organisms.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Julian et al. (Aug 1998).

Julian et al. (Aug 1998) discloses using HPLC-ESI-MS to profile uncharacterized crude extracts from eighty eight filamentous fungal cultures. In this manner a library of data is obtained.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smedsgaard et al. (1996) and Julian et al. (Aug 1998) in view of Demirev et al. (1999), Hathout et al. (1999), Leenders et al. (1999), Jarman et al. (2000), Erhard et al. (1997), Arnold et al. (1998), Heller et al. (1987), Claydon et al. (1996), Liang et al. (1996), and Krishnamurthy et al. (1996).

The teachings of Smedsgaard et al. (1996) and Julian et al. (Aug 1998) have been discussed above. Smedsgaard et al. (1996) and Julian et al. (Aug 1998) lack MALDI and MALDI-TOF MS, all the specific matrix agents and the number of laser shots.

Demirev et al. (1999), Hathout et al. (1999), Leenders et al. (1999), Jarman et al. (2000), Arnold et al. (1998), Heller et al. (1987), Claydon et al. (1996), Erhard et al. (1997), Liang et al. (1996), and Krishnamurthy et al. (1996) teach bacterial or cyanobacterial identification and differentiation by profiling metabolites using MALDI, MALDI-TOF, or Fast Atom Bombardment mass spectroscopy. MALDI and MALDI-TOF sample preparations include use of TFA. Spectra are obtained from averages of 50-200 shots. Wavelength used was 337 nm with proteins and peptides. Matrix acids may be sinapinic acid or  $\alpha$ -cyano-4-hydroxycinnamic acid (Demirev; Leenders; Arnold), 2,5-dihydroxybenzoic acid (Hathout). Demirev indicates that the method is not limited to the specific sample preparation and instrumentation exemplified (page

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2733). Erhard indicate that they were led to this method because of the success in using it with ordinary bacteria.

A person of ordinary skill in the art at the time the invention was made would have been motivated to substitute the known matrix acids and laser shots disclosed by Demirev et al. (1999), Hathout et al. (1999), Leenders et al. (1999), Erhard et al. (1997), Jarman et al. (2000), Arnold et al. (1998), Heller et al. (1987), Claydon et al. (1996), Liang et al. (1996), and Krishnamurthy et al. (1996) for those of Smedsgaard et al. (1996) and Julian et al. (Aug 1998) because of the wide experience evidenced in profiling metabolites from microorganisms with these methods. Both groups are solving the same problem, profiling microorganisms with MS for rapid identification. Bacteria or fungi are expected to have unique identifiers that does not depend on their being bacteria or fungi. Both kinds of organisms have cell walls as well as outer membranes. The tremendous experience of identifications with MALDI and MALDI-TOF with bacteria strongly suggests that the same methods will be equally applicable to fungi, and this is the basis of Erhard in going from bacteria to cyanobacteria. Many of these references indicate that the method is applicable to "microorganisms." Arnold, for example, indicate that their profiling method could be applied to other problems. The number of laser shots appears to be an arbitrary matter of experimental design choice dictated by the nature and concentration of the sample available. The choice of a specific matrix agent appears to be an arbitrary matter of experimental design choice having to do with the specific sample metabolites being considered.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute the matrix agents of Demirev et al. (1999), Hathout et al. (1999), Leenders et al. (1999), Erhard et al. (1997) and Arnold et al. (1998) for those of

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Smedsgaard et al. (1996) and Julian et al. (Aug 1998) and to vary the number of laser shots as needed in a MALDI or MALDI-TOF generation of identifying biomarkers database.

Other references cited by examiner but not relied upon are cited to establish the state of the art. Ho et al. (1998), Ryzhov et al. (2000), Fox et al. (1993), Goodacre et al. (1999), are all directed to a method for generating and MS identifying biomarkers for various bacteria. Li et al. (Jul 2000), Valentine et al. (2002), Wilkins et al. (Dec 2000), and Amiri-Eliasi et al. (Nov 2001) while directed to a method for generating and MS identifying biomarkers for various fungi or pollen do not qualify as prior art.

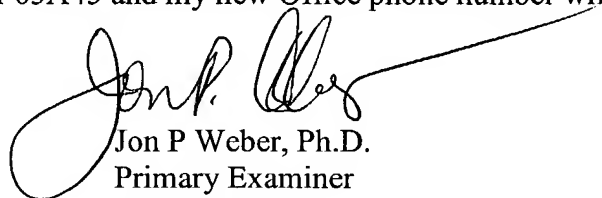
No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon P Weber, Ph.D. whose telephone number is 703-308-4015. The examiner can normally be reached on daily, off 1st Fri, 9/5/4.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 703-308-4743. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

My new Office room number will be Rem-03A45 and my new Office phone number will be 571-272-0925 after 15 January 2004.

  
Jon P Weber, Ph.D.  
Primary Examiner  
Art Unit 1651

JPW  
13 January 2004